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WHAT IS CLAIMED IS:

- 1 1. An isolated DNA molecule selected from the group consisting of:
  - 2 A. the DNA sequence of FIGURE 1 (SEQ ID NO:1);
  - 3 B. the DNA sequence of FIGURE 2 (SEQ ID NO:3);
  - 4 C. the DNA sequence of FIGURE 20A (SEQ ID NO:22);
  - 5 D. DNA sequences that hybridize to any of the foregoing DNA sequences
  - 6 under standard hybridization conditions;
  - 7 E. DNA sequences that code on expression for an amino acid sequence
  - 8 encoded by any of the foregoing DNA sequences;
  - 9 F. degenerate variants thereof;
  - 10 G. alleles thereof; and
  - 11 H. hybridizable fragments thereof.
- 1 2. An isolated nucleic acid molecule, which nucleic acid molecule encodes an  
2 ob polypeptide, which polypeptide is characterized by having about 145 to about  
3 167 amino acid residues, being expressed predominantly by adipocytes, and being  
4 capable of inducing a reduction of body weight in an animal.
- 1 3. The isolated nucleic acid of Claim 2, wherein the ob polypeptide has an  
2 amino acid sequence selected from the group consisting of the sequence depicted  
3 in:
  - 4 a) Figure 1 (SEQ ID NO:2),
  - 5 b) Figure 1 from amino acid number 22 to amino acid number 167, Figure 3  
6 (SEQ ID NO:4),
  - 7 c) Figure 3 from amino acid number 22 to amino acid number 167,
  - 8 d) Figure 5 (SEQ ID NO:5),
  - 9 e) Figure 5 from amino acid number 22 to amino acid number 166,
  - 10 f) Figure 6 (SEQ ID NO:6), and
  - 11 g) Figure 6 from amino acid number 22 to amino acid number 166.

1 4. The nucleic acid molecule of Claim 2 selected from the group consisting of  
2 DNA and RNA.

1 5. The nucleic acid molecule of Claim 2, which has a sequence as shown in  
2 Figure 1 (SEQ ID NO:1) from nucleotide number 46 to nucleotide number 550.

1 6. The nucleic acid molecule of Claim 2, which has a sequence as shown in  
2 Figure 2 (SEQ ID NO:2) from nucleotide number 46 to nucleotide number 550.

1 7. The nucleic acid molecule of Claim 1 which is detectably labeled.

1 8. A vector, which comprises the DNA molecule of Claim 1.

1 9. An expression vector, which comprises the nucleic acid molecule of Claim  
2 2, operatively associated with an expression control sequence.

1 10. A nucleic acid hybridizable to a non-coding region of an *ob* nucleic acid,  
2 which non-coding region is selected from the group consisting of an intron, a 5'  
3 non-coding region, and a 3' non-coding region.

1 11. A probe capable of screening for a nucleic acid encoding an *ob*  
2 polypeptide, which probe is a labeled DNA molecule of Claim 1.

1 12. A unicellular host transfected with a cloning vector of Claim 8.

1 13. A unicellular host transfected with an expression vector of Claim 9.

1 14. The unicellular host of Claim 13 wherein the unicellular host is selected  
2 from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, *Pichia*  
3 yeasts, CHO, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, and BMT10 cells,  
4 plant cells, insect cells, and human cells in tissue culture.

1 15. An oligonucleotide primer for amplifying human genomic DNA encoding  
2 an ob polypeptide.

1 16. The oligonucleotide of Claim 15, which is selected from the group  
2 consisting of

3 HOB 1gF 5'-CCCAAGAAGCCCATCCTG-3' (SEQ ID NO:26)  
4 HOB 1gR 5'-GACTATCTGGTCCAGTGCC-3' (SEQ ID NO:27)  
5 HOB 2gF 5'-CCACATGCTGAGCACTTGT-3' (SEQ ID NO:28)  
6 HOB 2gR 5'-CTTCAATCCTGGAGATACTGG-3' (SEQ ID NO:29).

1 17. An ob polypeptide, which polypeptide is encoded by the DNA molecule of  
2 Claim 1.

1 18. An ob polypeptide, which polypeptide is characterized by having about 145  
2 to about 167 amino acid residues, being expressed predominantly by adipocytes,  
3 and being capable of inducing a reduction of body weight in an animal.

1 19. The ob polypeptide of Claim 18 which has the amino acid sequence shown  
2 in Figure 1 (SEQ ID NO:2) or Figure 5 (SEQ ID NO:5).

1 20. The ob polypeptide of Claim 19 which has the amino acid sequence shown  
2 in Figure 3 (SEQ ID NO:4) or Figure 6 (SEQ ID NO:6).

1 21. An immunogenic fragment of an ob polypeptide, which polypeptide is  
2 characterized by having about 160 amino acid residues, being expressed  
3 predominantly by adipocytes, and being capable of inducing a reduction of body  
4 weight in an animal.

1 22. The immunogenic fragment of an ob polypeptide of Claim 21, which is  
2 selected from the group consisting of

3       Val-Pro-Ile-Gln-Lys-Val-Gln-Asp-Asp-Thr-Lys-Thr-Leu-Ile-Lys-Thr (SEQ ID  
4       NO:18);  
5       Leu-His-Pro-Ile-Leu-Ser-Leu-Ser-Lys-Met-Asp-Gln-Thr-Leu-Ala (SEQ ID  
6       NO:19);  
7       Ser-Lys-Ser-Cys-Ser-Leu-Pro-Gln-Thr-Ser-Gly-Leu-Gln-Lys-Pro-Glu-Ser-Leu-  
8       Asp (SEQ ID NO:20); and  
9       Ser-Arg-Leu-Gln-Gly-Ser-Leu-Gln-Asp-Ile-Leu-Gln-Gln-Leu-Asp-Val-Ser-Pro-  
10      Glu-Cys (SEQ ID NO:21).

1       23.    A derivative of a polypeptide according to claim 17 or 18 having one or  
2       more chemical moieties attached thereto.

1       24.    The derivative of claim 15 wherein the chemical moiety is a water soluble  
2       polymer.

1       25.    The derivative of claim 16 wherein the water soluble polymer is  
2       polyethylene glycol.

1       26.    An analog of an ob polypeptide having the amino acid sequence of human  
2       ob depicted in Figure 4, which analog is selected from the group consisting of:  
3       A. serine residue at position 53 substituted with glycine, alanine, valine,  
4       cysteine, methionine, or threonine;  
5       B. serine residue at position 98 substituted with glycine, alanine, valine,  
6       cysteine, methionine, or threonine;  
7       C. arginine residue at position number 92 substituted with asparagine, lysine,  
8       histidine, glutamine, glutamic acid, aspartic acid, serine, threonine, methionine, or  
9       cysteine;  
10      D. one or more of residues 121 to 128 substituted with glycines or alanines;  
11      E. deletion of one or more amino acid residues at positions 121-128;  
12      F. a loop structure formed by the disulfide bond that forms between cysteine  
13      residues 117 and 167;

- 14      G. amino acids from residue 22 to 53;
- 15      H. amino acids from residue 61 to amino acid residue 116;
- 16      I. amino acids from residue 61 to amino acid residue 167;
- 17      J. aspartic acid at one or more of residues 29, 30, 44, 61, 76, 100, and 106
- 18      substituted with glutamic acid; and
- 19      K. one or more isoleucine residues substituted with leucine.

1      27. A method for preparing an ob polypeptide comprising:  
2      A. culturing a unicellular host of Claim 12 or 13 under conditions that provide  
3      for expression of the ob polypeptide; and  
4      B. recovering the expressed ob polypeptide.

5      28. The method according to Claim 27 wherein the host cell is a bacterium.

1      29. The method according to Claim 27, wherein the host cell is a yeast.

1      30. The method according to Claim 27, further comprising:  
2      C. chromatographing the polypeptide on a Ni-chelation column; and  
3      D. purifying the polypeptide by gel filtration.

1      31. The method according to Claim 30, further comprising after step C and  
2      before step D chromatographing the ob polypeptide on a strong cation exchanger  
3      column.

1      32. An antibody to the ob polypeptide of Claim 17.

1      33. An antibody to the ob polypeptide of Claim 18.

1      34. A method for preparing an antibody to an ob polypeptide, comprising:  
2      A. conjugating the immunogenic fragment of an ob polypeptide of Claim 19 to  
3      a carrier protein;

4        B. immunizing a host animal with the ob polypeptide fragment-carrier protein  
5        conjugate of step A admixed with an adjuvant; and  
6        C. obtaining antibody from the immunized host animal.

1        35. The antibody of Claim 32, 33, or 34 which is a polyclonal antibody.

1        36. The antibody of Claim 32, 33, or 34 which is a monoclonal antibody.

1        37. An immortal cell line that produces a monoclonal antibody according to  
2        Claim 36.

1        38. The antibody of Claim 32, 33, or 34 labeled with a detectable label.

1        39. A method for measuring the presence of an ob polypeptide in a sample,  
2        comprising:

3        A. contacting a sample suspected of containing an ob polypeptide with an  
4        antibody that binds to the ob polypeptide under conditions which allow for the  
5        formation of reaction complexes comprising the antibody and the ob polypeptide,  
6        B. detecting the formation of reaction complexes comprising the antibody and  
7        ob polypeptide in the sample;  
8        in which detection of the formation of reaction complexes indicates the presence of  
9        ob polypeptide in the sample.

1        40. The method of Claim 39 in which the antibody is bound to a solid phase  
2        support.

1        41. A method for evaluating the level of ob polypeptide in a biological sample

2        comprising

3        A. detecting the formation of reaction complexes in a biological sample  
4        according to the method of Claim 30; and

5       B. evaluating the amount of reaction complexes formed, which amount of  
6 reaction complexes corresponds to the level of ob polypeptide in the biological  
7 sample.

1   42.   A method for detecting or diagnosing the presence of a disease associated  
2 with elevated or decreased levels of ob polypeptide in a mammalian subject  
3 comprising:

4       A. evaluating the level of ob polypeptide in a biological sample from a  
5 mammalian subject according to Claim 41; and

6       B. comparing the level detected in step (A) to a level of ob polypeptide  
7 present in normals or in the subject at an earlier time;  
8 in which an increase in the level of ob polypeptide as compared to normal levels  
9 indicates a disease associated with elevated levels of ob polypeptide, and decreased  
10 level of ob polypeptide as compared to normal levels indicates a disease associated  
11 with decreased levels of ob polypeptide.

1   43.   A method for monitoring a therapeutic treatment of a disease associated  
2 with elevated or decreased levels of ob polypeptide in a mammalian subject  
3 comprising evaluating the levels of ob polypeptide in a series of biological samples  
4 obtained at different time points from a mammalian subject undergoing a  
5 therapeutic treatment for a disease associated with elevated or decreased levels of  
6 ob polypeptide according to the method of Claim 41.

1   44.   A method for changing the body weight of a mammal comprising inhibiting  
2 the expression of an ob polypeptide encoded by a nucleic acid of Claim 2.

1   45.   The method according to Claim 44 comprising expressing an antisense  
2 nucleic acid molecule hybridizable to a nucleic acid that expresses the ob  
3 polypeptide, expressing a ribozyme that cleaves a nucleic acid that expresses the  
4 ob polypeptide, administering an antisense nucleic acid molecule hybridizable to a

5 nucleic acid that expresses the ob polypeptide, and administering a ribozyme that  
6 cleaves a nucleic acid that expresses the ob polypeptide.

1 46. A pharmaceutical composition for reducing body weight of an animal  
2 comprising the ob polypeptide of Claim 17 and a pharmaceutically acceptable  
3 carrier.

1 47. A pharmaceutical composition for reducing body weight of an animal  
2 comprising the ob polypeptide of Claim 18 and a pharmaceutically acceptable  
3 carrier.

1 48. A method for reducing the body weight of an animal comprising  
2 administering an amount of a pharmaceutical composition of Claim 47 effective to  
3 reduce the body weight of an animal to an animal believed to be in need of  
4 decreased body weight.

1 49. The method according to Claim 48 wherein the animal is a human, and the  
2 ob polypeptide is human ob polypeptide.

1 50. A method for reducing the body weight of a mammal comprising increasing  
2 the expression of a protein encoded by the nucleic acid of Claim 2.

1 51. A pharmaceutical composition for increasing the body weight of an animal  
2 comprising an antagonist of an ob polypeptide.

1 52. The pharmaceutical composition of Claim 51, wherein the antagonist is  
2 selected from the group consisting of an antibody that binds to and neutralizes the  
3 activity of ob polypeptide, a fragment of the ob polypeptide that binds to but does  
4 not activate the ob receptor, and a small molecule antagonist of the ob  
5 polypeptide.

- 1 53. A method for increasing the body weight of an animal comprising
- 2 administering an amount of the pharmaceutical composition of Claim 51 effective
- 3 to cause an increase in body weight to an animal believed to be in need of
- 4 increased body weight.